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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,396	07/30/2001	Brian Kennedy	20162PDA	1405

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,396	KENNEDY ET AL.	
	Examiner	Art Unit	
	Thai-An N Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/31/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' Amendment and Response, filed 10/07/03 has been entered. Claim 23 has been cancelled. Claim 22 is pending and under current examination.

Priority

If applicant desires priority under 35 U.S.C. 119(e) and 120 based upon a previously filed application(s), specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and

(a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claim 22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is *maintained* for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that, "[A]pplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar,* 19USPQ2d at 1117. The specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

Applicants disagree with prior rejection. They submit that the entire specification is directed to methods of identification of PTP-1B inhibitors. Applicants point to the specification which describes a mouse model which would be used to identify inhibitors. Applicants further argue that the present invention provides a method for identifying the inhibitors of enzymatic activity of PTP-1B, and methods of screening or identifying inhibitors of enzymatic activity of PTP-1B protein by transfecting a cell with DNA encoding the human PTP-1B protein, as well as a method of determining whether a substance regulates obesity in a mammal. See pp. 4-5 of the Response.

Applicants' arguments are not persuasive. The specification describes general methods for the identification of inhibitors of PTP-1B and methods of utilizing inhibitors identified by such methods. However, the specification fails to describe any particular inhibitor of PTP-1B with particularity to indicate that Applicants had possession of the claimed invention. The claimed invention as a

whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that one of skill in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998).

It is reiterated that claim 22 indicates that the inhibitor of PTP-1B is critical and essential to the practice of the claimed invention. The specification teaches methods for the identification of inhibitors of the enzymatic activity of PTP-1B [see pp. 13-14]. However, the skilled artisan cannot envision the detailed chemical structure of all the inhibitors of PTP-1B enzymatic activity, as encompassed by the claims, and therefore, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The

specification provided only the bovine sequence. The instant claim requires an inhibitor but there is no description of inhibitors of PTP-1B, which would indicate possession by Applicant at the time of filing.

Therefore, as no inhibitors of the enzymatic activity of PTP-1B have been described, the claim does not meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claim 22 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is *maintained* for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is directed to a method of treating obesity comprising administering an inhibitor of the enzymatic activity of PTP-1B to an obese mammal.

Applicants argue that MPEP §2107.03 states that it is improper for the Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness. See p. 6, 3rd ¶ of the Response. Applicants argue that the instant rejection is improper. Applicants further argue that the KO mouse described in the specification has a remarkably normal phenotype, and that this provides evidence that an inhibitor is not likely to cause grievous harm. Further, Applicants argue that because the phenotype at issue is so benign, the therapeutic window is not so narrow, therefore, choosing a precise dosing regimen for weight reduction is not critical to the invention. Applicants state that this is a clear advantage in the treatment of any disease and thus, there would be no undue experimentation associated with dosage selection of the present invention. See pp. 7-8 of the Response.

Applicants' arguments are not persuasive. Although the specification teaches general methods for the identification of inhibitors, the specification fails to teach or provide guidance for the correlation between the administration of an identified inhibitor of PTP-1B to an obsess mammal and the treatment of obesity in the animal. MPEP §2164.03 states that:

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art.

It is well-known in the art that causes of obesity are multi-faceted, stemming from both genetic and environmental factors, and treatment of obesity is complicated and unpredictable. Friedman [**Science**, 299:856-858 (2003)] teaches that, "Thus, one might ponder why, in our current environment where almost everyone has essentially free access to calories, anyone is thin. The answer appears to reside in our genes, and the way in which they interact with environmental factors." See col. 2-3, bridging ¶. Friedman further states, "In any individual's case, genetic factors play a role in determining body size but tend to cancel out in large samples from a genetic pool, leaving levels and trends in body size that result from environmental factors." See col. 3, 2nd ¶. With regard to treatment of obesity, Friedman states that, "Our approach to the obesity epidemic should be analogous: Identify the molecular components of the system that regulates body weight, define what is different about the system in lean and obese subjects, and elucidate how environmental and developmental factors alter the function of this system. Such a foundation is essential for the development of rational therapies." See p. 258, 3rd column. Holm *et al.* [**J. of Adv. Nurs.**, 36(2):266-269 (2001)] state that the cause for

the rise in obesity throughout the world is attributed to better living standards [see p. 267, 2nd column, 3rd ¶] and that many societal factors create, promote and maintain obesity [see pp. 267-268]. The specification teaches that the PTP-1B knockout mice of the invention, when fed a high fat, high carbohydrate diet, are more insulin-sensitive but obesity resistant. The specification fails to teach the administration of an inhibitor of the enzymatic activity of PTP-1B to an obese mammal would result in treatment of obesity. The specification fails to show that administration of such an inhibitor would result, for example, in weight loss. The state of the art supports that because the cause for obesity is both environmental and genetic, it would be unpredictable that the administration of an inhibitor of PTP-1B would be sufficient to treat obesity, as required by the claims.

Accordingly, in view of the specification's lack of teachings, guidance, or working examples with regard to the treatment of an obese mammal by administration of an inhibitor of PTP-1B, the specification's lack of correlation between administration of an inhibitor of PTP-1B and the treatment of obesity in a mammal, the state of the art, which teaches that obesity is caused by multiple factors, and that treatment of obesity requires consideration of both environmental and genetic factors, it would have required undue experimentation for one of skill in the art to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The prior rejection of claim 22, as vague and indefinite, is *maintained.* Applicants argue that the claim is definite in that it sets forth the active, positive step of administering an inhibitor of the enzymatic activity of PTP-1B to an obese mammal. Applicants argue that while multiple steps are recited, the claimed step is clear. Applicants further argue that the term "inhibitor" is well-known and understood in the art and provide a definition from Webster's dictionary. Applicants argue that thus, it would be clear that an inhibitor the enzymatic activity of PTP-1B would be an agent that restrains or retards the enzymatic activity of PTP-1B.

Applicants' arguments are found to be partially persuasive. The Examiner agrees that the term "inhibitor" would be definite. However, the claim is indefinite because it provides no clear method steps. For example, it is unclear how administering an inhibitor of PTP-1B to an obese mammal relates to the preamble of the claim, "A method of treating obesity."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be

patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ahmad *et al.*, [J. Clin. Invest., 100(2):449-458 (1997)] when taken with Puius *et al.* [PNAS, 94:13420-13425 (1997)].

Ahmad teaches that obese human subjects have increased protein-tyrosine phophatase [PTPase] activity in their adipose tissue that can dephosphorylate and inactivate the insulin receptor kinase. They teach that PTPase activity was measured in the skeletal muscle of lean controls, insulin-resistant obsess non-diabetic subjects and obese subjects with non-insulin-dependent diabetes. See *Abstract* and *Methods*, p. 450. They teach that in obese, nondiabetic subjects, PTP1B was increased by 1.9 fold in the muscle cytosol. See Figure 5 and p. 453, 2nd

column, 1st full ¶. Further, that PTP1B negatively regulates insulin receptor activation, and that, "Since PTP1B has a role in the negative regulation of insulin signaling and acts, at least in part, directly at the level of the receptor kinase, it may function in concert with LAR [leukocyte antigen related] in the physiological regulation of the insulin receptor." See p. 456, 2nd ¶. Ahmad does not teach the inhibition of PTP-1B.

However, Puius teach that PTPases have a sequence specificity that can be exploited in the design of potent and selective PTPase inhibitors. See p. 13420, 1st column, 1st ¶, lines 15-18. They teach that PTP1B is implicated as a negative regulator of insulin-stimulated pathways and that the structure of PTP1B's active sites, "[H]ave significant implications for PTP1B inhibitor design, as it should be possible to develop compounds that can simultaneously occupy both sites to gain higher affinity and selectivity." See p. 13420, 2nd ¶, last sentence.

Accordingly, in view of the combined teachings, it would have been obvious for one of skill in the art to administer an inhibitor of the enzymatic activity of PTP-1B to an obese mammal. One of skill in the art would have been motivated in order to test various inhibitors the PTP-1B. Note that absent any required effect on the obese mammal the claimed invention is rendered obvious by combination of the teachings of the prior art.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Note: After January 13, 2004, the Examiner may be reached at (571) 272-0736. If the Examiner is unavailable, inquiries may be directed to Deborah Reynolds, SPE of Art Unit 1632, at (571) 272-0734.

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